UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/743,516	01/31/2001	Martin Braddock	1430-261	4022

23347 7590 11/03/2003

DAVID J LEVY, CORPORATE INTELLECTUAL PROPERTY
GLAXOSMITHKLINE
FIVE MOORE DR., PO BOX 13398
RESEARCH TRIANGLE PARK, NC 27709-3398

EXAMINER	
PRIEBE, SCOTT DAVID	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/743,516	BRADDOCK ET AL.	
	Examiner	Art Unit	
	Scott D. Priebe	1632	

-- The MAILING DATE of this communication app ars on the cover sheet with th correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,23-38,40 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,23-38,40 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 10/7/03 has been entered. Claims 15, 23-38 were pending. Claims 15 and 23-26 have been amended, claims 40 and 41 have been added. The amendment provided in the submission does not comply with 37 CFR 1.121. Claims 24 and 25 are not "original" as indicated. The text of current claims 24 and 25 is identical to previous claims 23 and 24, respectively, and therefore lacks underlining of newly added material and the presence of deleted material marked by strikethrough.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 23, 25-38, and 41 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well-established utility.

These claims are explicitly directed to a method for reducing angiogenesis associated with wound healing. As indicated in the specification, angiogenesis is a natural and necessary process in wound healing. The specification asserts no practical use for such a method, nor any benefit to the public for such a method in a real world context, nor is there any evidence of record for a well-established use for such a method. While such a method may have some value as an object of basic research, such a use does not meet the requirements of §101.

Claims 23, 25-38, and 41 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

Claims 15, 23, 25-38, 40, and 41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 15, 23, and 25-38 have been amended to include limitations not previously recited. Claims 40 and 41 are new claims which include new limitations. Applicant has not indicated where or how the original specification supports these limitations, as is Applicant's burden. MPEP 714.02, last sentence of the third paragraph from the end and 2163.06 (I), last sentence.

Claim 15 has been amended to indicate that the claimed method is used "for improved wound healing in a mammal". The original specification described the method as being one for inhibiting or reducing cell proliferative disorders associated with wound healing. The term "improved" is subjective, and may embrace any number of results in wound healing beyond the scope of the inhibiting or reducing cell proliferative disorders. While one might accept that reduction of undesired cell proliferation in wound healing is an improvement, e.g. reducing keloid formation, it is certainly not commensurate with an unspecified "improvement". Accelerated wound healing might also be considered to be "improved wound healing"; however, the specification teaches against this (page 29, lines 18-23). There is no evidence of record that any other types of "improved wound healing" were contemplated, nor that Applicant was in possession of any methods directed to such.

Claims 23, 25-38, and 41 are directed to a method of reducing angiogenesis associated with wound healing. The only part of the original specification that describes angiogenesis in a mammal is in the context of Example 4 where it was examined as an indication of whether exogenous Nab2 expression would repress growth factor activation. Nowhere does the specification describe, even in passing, that the disclosed method had use in inhibiting angiogenesis as the ultimate goal. Nowhere does the specification disclose administering a nucleic acid encoding Nab1 for such a purpose, and nowhere does the specification describe reducing angiogenesis outside the context of the specific conditions described Example 4. Furthermore, as shown in Fig. 4d, angiogenesis was reduced only in comparison to situations where other pretreatments had been administered. Angiogenesis was still increased relative to a

control where no pretreatment had been made, i.e. pretreatment with plasmid expressing Nab2 increased angiogenesis near a wound.

Claim 40 is directed to a method for suppressing expression levels of "transforming factor beta (TGFb) scarring growth factors" during wound healing by preadministering a nucleic acid encoding Nab2 at a site in which a wound will be made. The original specification provides no description of what "transforming factor beta (TGFb) scarring growth factors" are. The only mention in the original specification of pretreating a site of a future wound is made in Example 4. Figure 4 reports no findings on scarring whatsoever. It reports that TGFβ1 levels were reduced for treatment with Nab2 plasmid as compared to where no pretreatment was provided. However, an examination of Fig. 4b shows that if there was any such a reduction epidermal tissue it was slight and not statistically significant. While Fig. 4c shows that TGFβ1 levels were higher, if any different, in granulation tissue relative to no pretreatment. In contrast, TGFβ3 levels were higher with the pretreatment.

Disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. See *In re Shokal*, 113 USPQ 283 (CCPA 1957); *Purdue Pharma L.P. v. Faulding Inc.*, 56 USPQ2d 1481 (CAFC 2000). The rejection of claims 23, 25-38, 40 and 41 would be overcome by limiting the claims to the particulars of Example 4. However, this would necessitate a rejection of claim 40 as well under §101, for similar reasons as set forth above.

Claim 15 and 23-38 remain rejected and claims 40 and 41 are rejected under 35 U.S.C. 112, first paragraph, for the reasons of record applied to claims 1-16 set forth in the

Office action of 1/18/02, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 15 has been amended to embrace using the claimed method for any general improvement in wound healing, rather than simply reducing cell proliferation disorders associated with wound healing, and the specification does not disclose any other type of improvement. Claim 24 is identical to previous claim 23. Claims 23, 25-38 and 41 are directed to methods for reducing angiogenesis associated with wounding. In addition to the specification failing to teach a use for such a method, the specification fails to enable achieving the goal of the method for the reasons of record. In addition, the results of Example 4, shown in Fig. 4d, suggest that pre-administration of the plasmid encoding Nab2 to the site of a future wound either had no effect or slightly increased angiogenesis when compared to a wound receiving no pretreatment.

Claim 40 is directed to a method for suppressing expression levels of "transforming factor beta (TGFb) scarring growth factors" during wound healing by preadministering a nucleic acid encoding Nab2 at a site in which a wound will be made. The original specification provides no description of what "transforming factor beta (TGFb) scarring growth factors" are. The only mention in the original specification of pretreating a site of a future wound is made in Example 4. Figure 4 reports no findings on scarring whatsoever. It reports that TGFβ1 levels were reduced for treatment with Nab2 plasmid as compared to where no pretreatment was provided. However, an examination of Fig. 4b shows that if there was any such a reduction epidermal tissue it was slight, and not statistically significant. In contrast, Fig. 4c shows that TGFβ1 levels were higher with the pretreatment, if any different, in granulation tissue. In contrast, TGFβ3 levels were

higher with pretreatment. The only potential use for the method disclosed in the original specification might be for reducing post-operative scarring. However, Example 4 presents no evidence that such pre-treatment with a plasmid encoding Nab2 would result in reduced scar formation. There is no evidence of record that use of any other type of vector would accomplish this either.

Applicant's arguments filed 10/7/03 have been fully considered but they are not persuasive. Applicant argues that if "site" is given plain meaning, then "wound site" would embrace the site of a future wound, e.g. as in Example 4. However, as indicated in previous Office actions, the original specification provides no guidance or direction to use the claimed method in the context of a future "wound site", other than perhaps Example 4. However, Example 4 is not presented as an example of a potential use of the claimed method, but rather as a preliminary experiment to examine the potential effects of Nab2 gene therapy. This is evident by the fact that the method is described in the original specification as being one for reducing undesired cell proliferation associated with wound healing, and Example 4 does not examine scar formation at all. In addition, even if the claims might embrace administration at the site of a future wound, claims 15 and 23-38 are not limited to such, nor has evidence been provided that the method would result in any therapeutically relevant effect in such a context. Applicant also argues that they are not required to determine optimal dosing regimens. No legal basis for this assertion is provided. Furthermore, this is not a simple issue of optimal dosing. In order for one to optimize a dose, one must have a starting dose known to yield at least a partial therapeutically relevant effect. Since no known effective dose is disclosed and no clearly effective set of treatment parameters is known, failure to achieve a therapeutically relevant outcome under a

given set of treatment parameters cannot be attributed to an insufficient dose, as opposed to some other problem or deficiency in the treatment parameters, such as timing. If the treatment under a given set of parameters fails, one of skill in the art has no way of predicting what parameter to vary in order to achieve at least partial success. The law under §112, first para. requires that the disclosure in the application shall inform those skilled in the art how to use the invention, not how to find out for themselves how to use it. *In re Gardner*, 166 USPQ 138, 141 (CCPA 1970).

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "improved" in claim 15 is a relative term which renders the claim indefinite. The term "improved" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear what result in wound healing would be an improvement, and therefore embraced by the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on 703 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

Primary Examiner
Art Unit 1632